

Radiation Epidemiology Course

Nuclear Accidents Part II: Chornobyl

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An aerial photograph of the Fukushima Daiichi nuclear power plant site, showing extensive destruction and debris. The image is overlaid with a semi-transparent blue filter. The text "Part I: Thyroid Cancer" is centered in a yellow font.

Part I: Thyroid Cancer

Thyroid Cancer Among Exposed Children

◆ Why Thyroid Cancer?

- Thyroid concentrates iodine (>> avg. body dose)
- Iodine deficient area
(however, treatment with ^{131}I apparently not a risk factor)

◆ Why Children?

- Rapid thyroid growth
- Small thyroid mass (inversely proportional to dose)
- More milk consumption

Study Designs

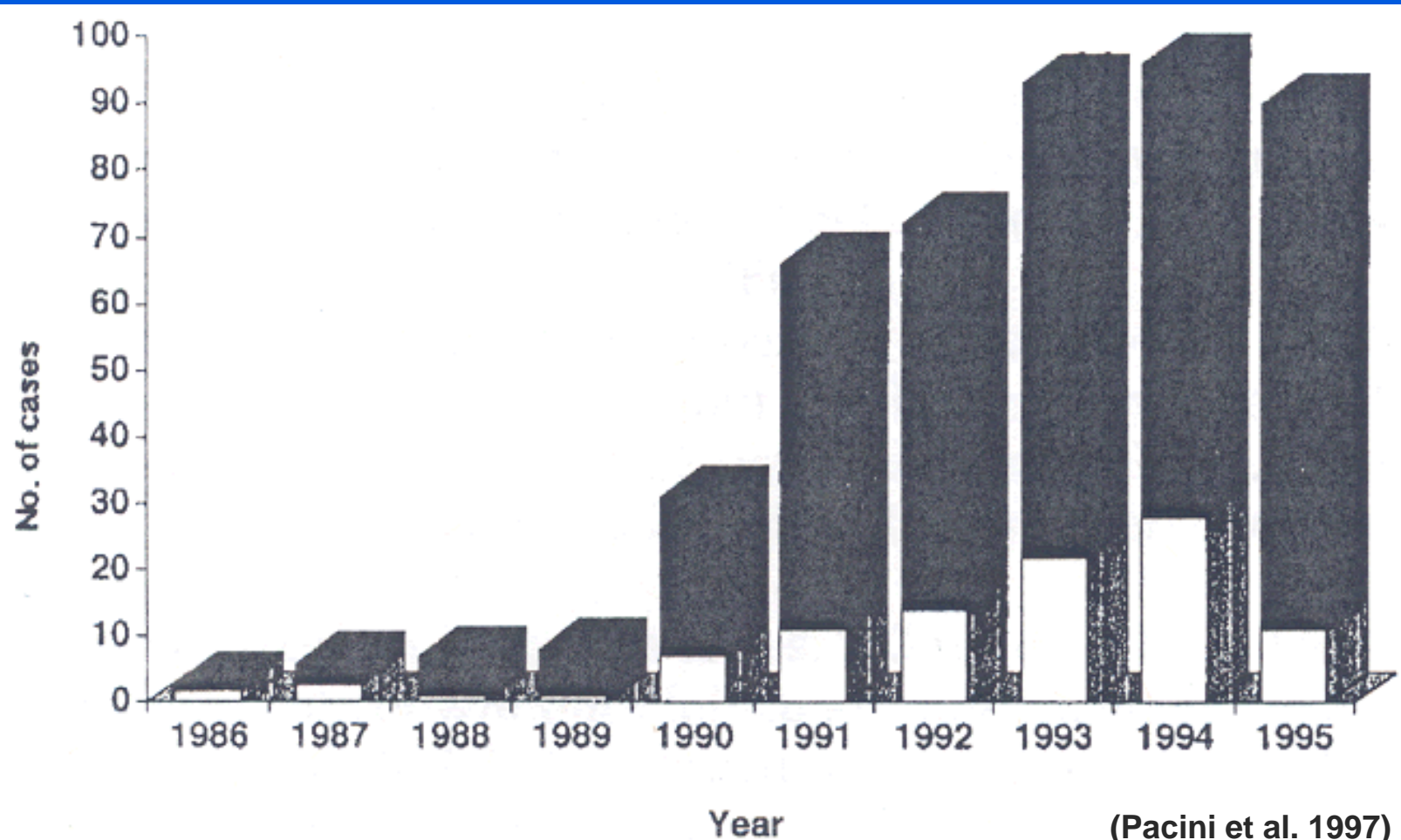
- ◆ **Ecologic Studies of temporal and geographic trends**
- ◆ **Analytic studies (case-control, cohort)**

Studies of Temporal and Geographic Trends

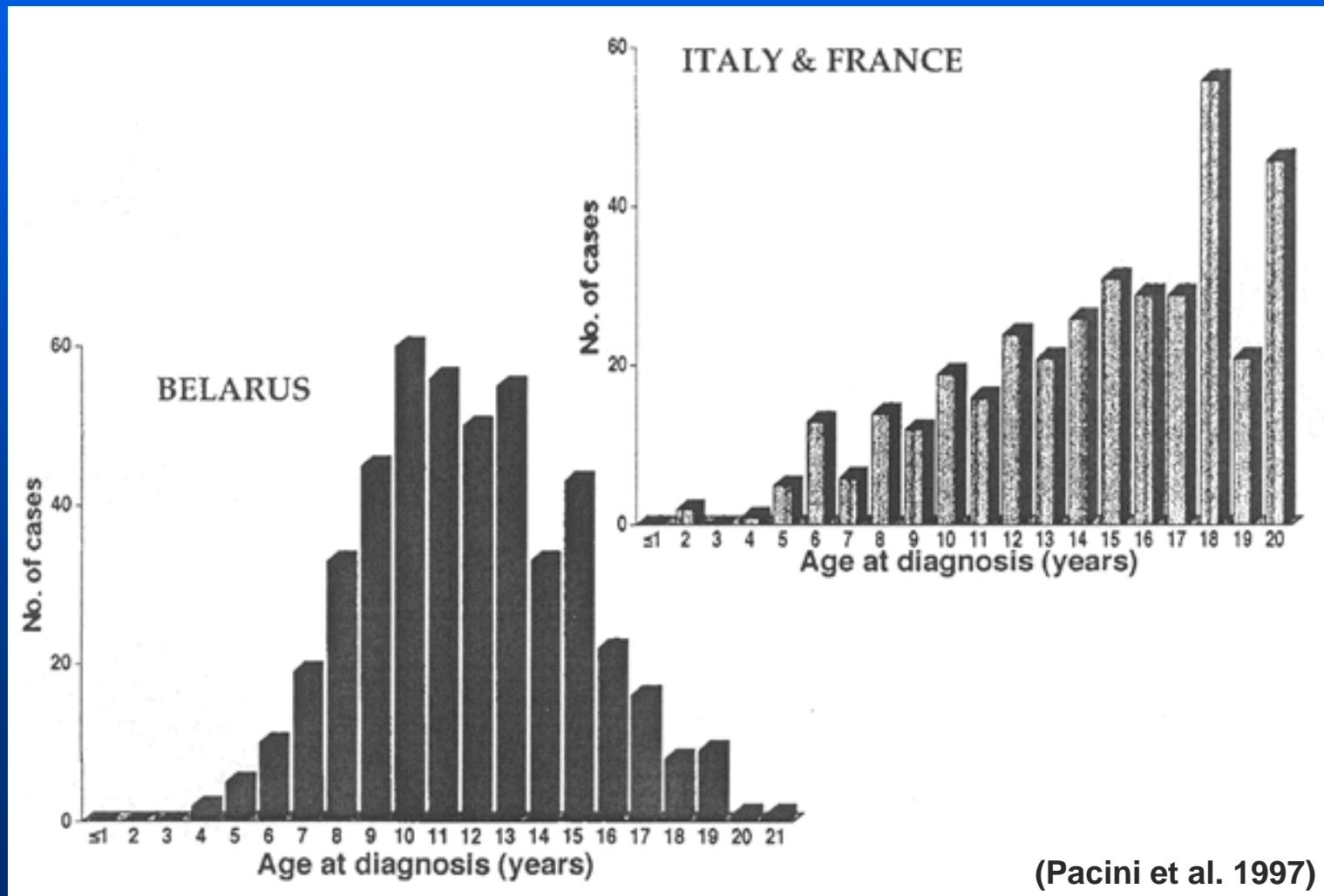
Descriptive Studies of Children < 18

- ◆ ~2000 cancers, 1990-98
- ◆ ≥ 4 -fold increase over earlier period, greatest in Gomel
- ◆ Short latency
- ◆ >92% papillary type (67% normative)
- ◆ Aggressive (solid or solid-follicular variant)

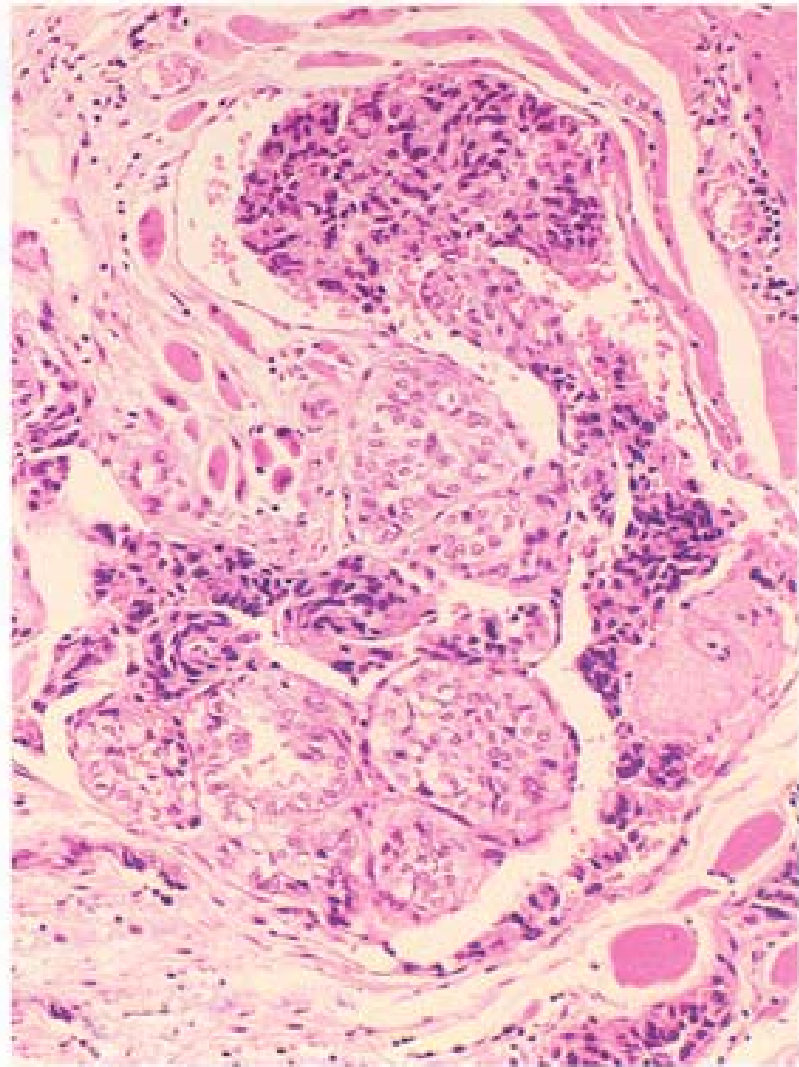
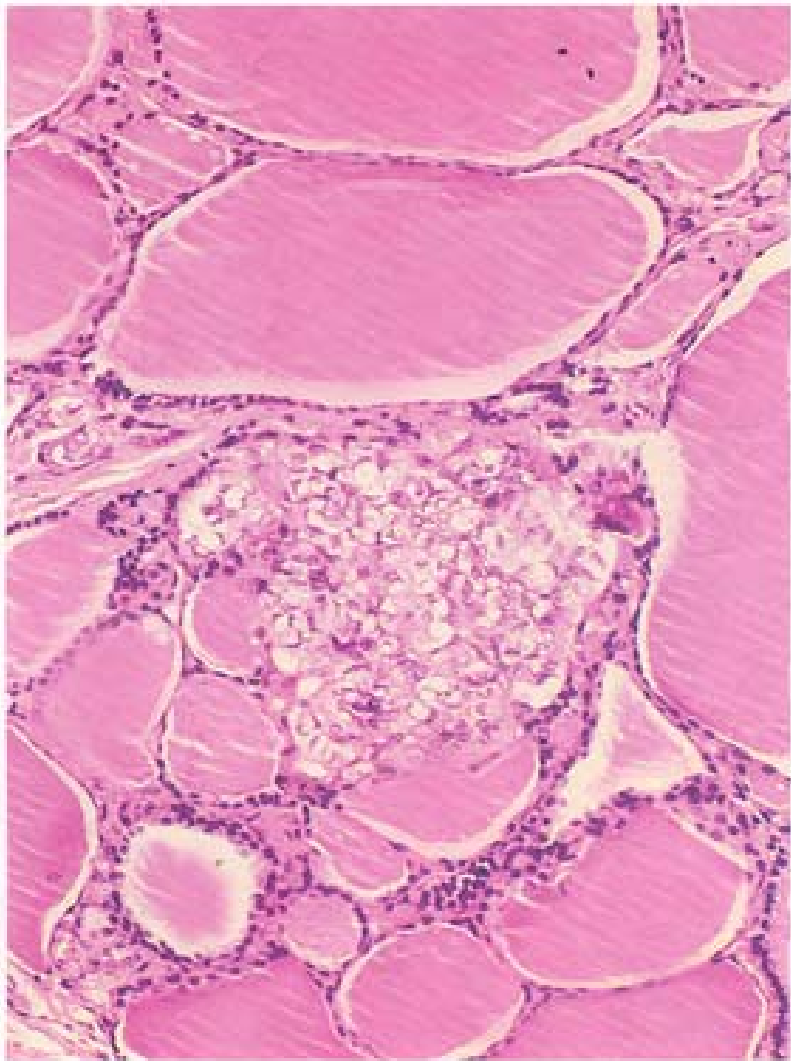
Cases of Childhood (■) and adolescent (□) thyroid carcinoma in Belarus, registered yearly from 1986- 1995



Age Distribution at the time of diagnosis of thyroid cancer patients from Belarus and from Italy and France



(Pacini et al. 1997)



Molecular Biology

- ◆ RET – PTC rearrangements
- ◆ Tyrosine kinase growth factor

Real effect
or
Screening effect?

Analytic Studies

Case Control Study in Belarus evaluating pathway to diagnosis

	Estimated Dose from ^{131}I (Gy)			OR (95% CI)
	<0.3	0.3 – 0.99	1.00 +	
Routine screening				2.08 (1.0 – 4.3)
Cases	32	16	15	
Controls	43	16	4	
Incidental finding				8.31 (1.1 – 5.8)
Cases	13	4	2	
Controls	18	1	0	
Enlarged or nodular thyroid				3.63 (0.7 – 1.8)
Cases	19	6	0	
Controls	23	2	0	
Incidental finding and enlarged or nodular thyroid				5.12 (1.4 – 1.8)
Cases	32	10	2	
Controls	31	3	0	

(Astakhova, et al. 1998)

Number of thyroid cancer cases after the Chornobyl accident by year (Belarus)

Year	Total
1986	3
1987	12
1988	9
1989	14
1990	38
1991	77
1992	100
1993	114
1994	146
1995	137
1996	156
1997	150
1998	165
1999	203
2000	171
Total	1,495

(Henigsberg, et al. 2002)

Ongoing Studies of Thyroid Cancer in Children

Ongoing studies include a single longitudinal cohort study - a collaboration between NCI, Columbia, Ukraine, and Belarus – and several case-control studies. They focus on the influence of age at exposure, gender, and iodine deficiency (among other variables) on the risk associated with ^{131}I exposure. All use individualized dose estimates.

Ongoing Studies

Ukrainian-American Thyroid Study Belarusian-American Thyroid Study

**A collaboration between scientists from
Ukraine, Belarus, NCI and Columbia University**



Approach

- ◆ **Longitudinal cohort study of exposed children involving detailed screening examinations of the thyroid gland every 2 years**
 - **Palpation**
 - **Ultrasound**
 - **Thyroid hormone and iodine measurements**

Description of Cohorts by Demographic Variables

	Belarus		Ukraine	
	N	%	N	%
Total	11,918	100.0	13,243	100.0
Gender				
Female	6,130	51	6,275	51
Male	5,788	49	6,518	49
Age on 26 April 1986 (years)				
0-4	3,866	33	4,037	31
5-9	3,500	29	3,836	29
10-14	3,109	26	4,145	31
≥ 15	1,443	12	1,225	9

Individual Dose Estimates

- ◆ **Thyroid activity measurement**
- ◆ **Dosimetry questionnaire**
- ◆ **Ecologic Model**

Preliminary Estimates:

Median : 0.3 Gy

Range : 1 mGy – 40 Gy

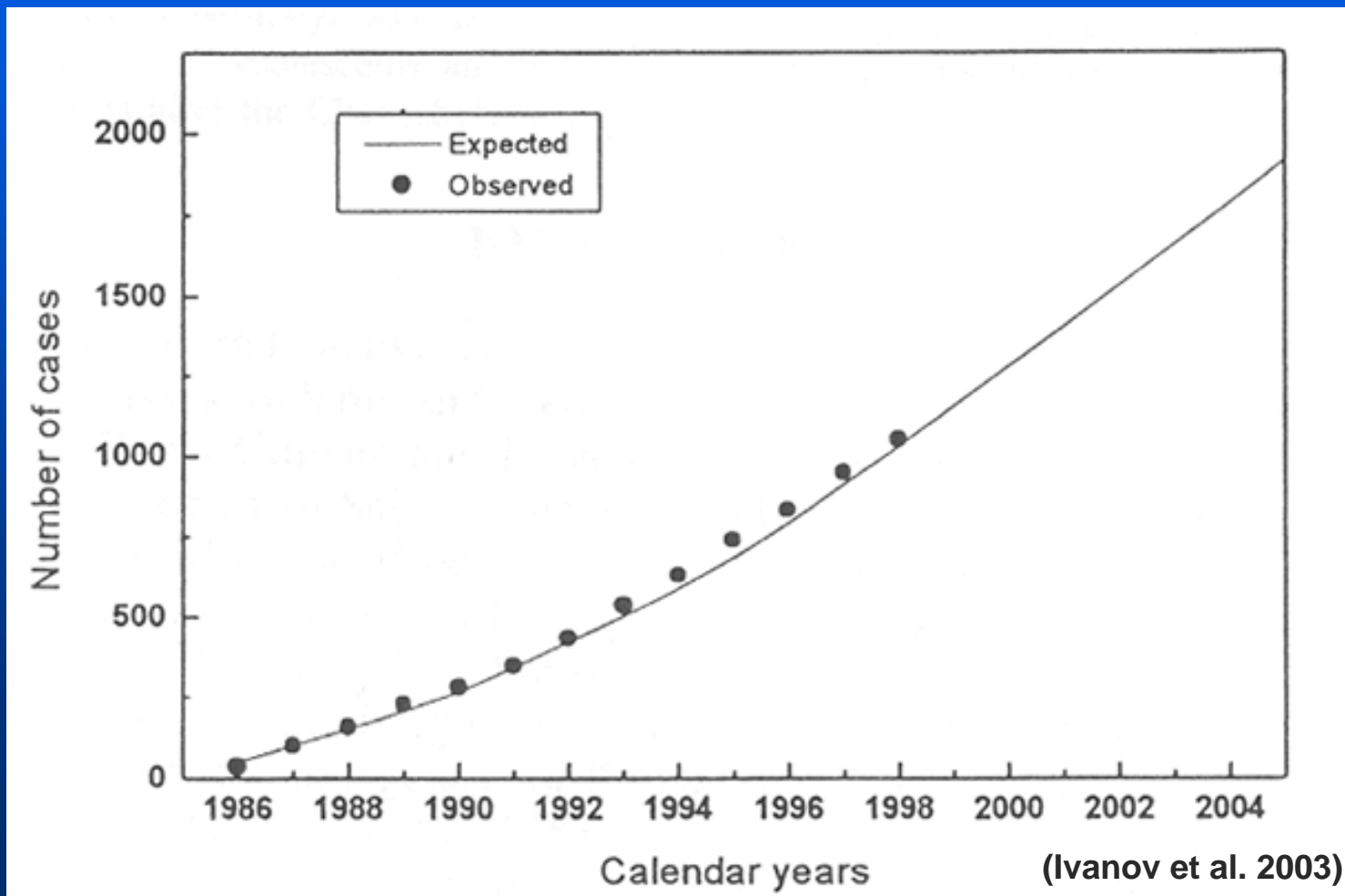
In Utero Substudy

- ◆ 1000 'exposed'
- ◆ 1000 'unexposed'

Benign and malignant nodules

Thyroid Cancer in Adults

Prediction of thyroid cancer incidence among adolescents and adults at the Chernobyl accident in the Bryansk region



Summary (1)

- ◆ **Thyroid cancer increased in exposed children, with risk greatest at youngest ages**
- ◆ **Tumors aggressive**
- ◆ **Increases still being seen**
- ◆ **Possible changes in histology and morphology over time**

Summary (2)

- ◆ **Molecular biology not certain and not certain if there is a Chornobyl footprint**
- ◆ **Risk of thyroid cancer in adults uncertain; may differ for clean-up workers and general population**

Importance of Chornobyl Studies

- ◆ **Will provide data on dose-response curve at low doses and low dose rates**

An aerial photograph of the Fukushima Daiichi nuclear power plant, showing the damaged reactor buildings and the containment dome. The image is overlaid with a blue filter. The text "Part II: Leukemia" is centered in the image.

Part II: Leukemia

Childhood Leukemia

Ecological Studies of temporal and geographical trends

- ◆ Cancer registries in 23 countries
- ◆ Dose estimated from fallout and intake of contaminated food
- ◆ Increases post-Chornobyl
- ◆ Excess not correlated with extent of contamination

(Parkin et al. 1993, 1996)

Childhood Leukemia

Analytic Studies

- ◆ Case-control study in contaminated oblasts of Ukraine
- ◆ Controls from different rayon than cases
- ◆ Increases in ALL (1993-97) and AML (1987-1982)
- ◆ Only 36% of cases included

(Noshchenko et al., 2002)

Leukemia in Children

- ◆ **Sole analytic study unconvincing due to potential selection bias**
- ◆ **Ecologic studies show temporal pattern but no geographic trend**
- ◆ **Evidence not strong for or against an association**

In Utero Exposure and Leukemia Risk

Ecological Studies of temporal and geographical trends

- ◆ Increase in risk for relevant birth cohort in Greece (July 1986 – December 1987)
(Petridou et al. 1996)
- ◆ Smaller increase in Germany
(Steiner et al. 1998)
- ◆ Increase in Belarus but trend weaker than in Greece
(Ivanov et al. 1998)

Exposed vs. Unexposed Birth Cohorts

Region	RR (95% CI)
Greece	2.6 (1.4 – 5.1)
Germany	1.5 (1.0 – 2.2)
Belarus	1.3 (0.8 – 2.1)
Mogilev & Gomel	1.5 (0.6 – 3.6)

(Ivanov et al. 1998)

Ecologic Studies (cont'd)

- ◆ **Comparison of cumulative incidence rates in children born in 1986 living in a contaminated vs. uncontaminated oblast in Ukraine**
- ◆ **Rates higher in exposed oblast**

(Noshchenko et al. 2002)

Cumulative incidence rates per 100,000, RR (95% CI) for leukemia by region and time, sexes combined

	1987-1991	1992-1996
Leukemia, all types, in children born in 1986		
Zhitomir (‘contaminated’)	11.2	4.4
Poltava (‘uncontaminated’)	5.7	0.8
Rate Ratio	1.9 (0.8 – 4.8)	5.5 (0.6 – 47)

(Noshchenko et al. 2002)

In Utero Exposure and Leukemia Risk

- ◆ **Some suggestive data but limitations prevent drawing strong conclusions**

Adult Leukemia

Clean-up Workers: Ecologic Studies

- ◆ No increased risk (Tukor & Dzagoeva 1993)
- ◆ No dose response (Shantyr et al. 1997)
- ◆ No trend with time (Buzunov et al 1996)
- ◆ Increased risks (Ivanov et al. 1997; 2003)

Adult Leukemia

Clean-up Workers: Analytic Studies

- ◆ 1 case-control study
(n=34 (non-CLL) cases)
- ◆ Controls matched on age, region
- ◆ RR elevated with duration of exposure (3.1) and dose (3.7) but not statistically significant

(Konogorov et al 2000)

Adult Leukemia

General Population: Ecologic Studies

- ◆ No evidence of an increase in most contaminated regions

(Ivanov et al. 1997; Bebeshko et al. 1997)

- ◆ No trend with time

(Prisyazhniuk et al. 1995)

Leukemia in Adults

- ◆ No evidence of an association in the general population
- ◆ Some slight evidence in clean-up workers (screening effect?)

Ongoing Studies

Ukrainian-American Study of Leukemia and Related Diseases Among Clean-up Workers from Ukraine Following the Chornobyl Accident

A collaboration among scientists from Ukraine, NCI and Columbia University



Study Design

- ◆ Cohort of 110,645 male clean-up workers from 30 km zone around plant, resident in study area
- ◆ Cases from all relevant sources assembled into a leukemia registry
- ◆ Five controls per case matched on age and area of residence
- ◆ Estimates of individual dose from detailed dosimetry interview

Bone Marrow Dose Estimates: Using RADRUE

- ◆ **RADRUE (Radiation Dose Reconstruction with Uncertainty Estimates) – time and motion analysis**
- ◆ **April 26, 1986 – December 31, 1990, 70 km zone**
- ◆ **Mission, episode, event, frame**
- ◆ **Expert assessment**

Preliminary Review

- ◆ **Leukemia (n=110)**
- ◆ **MM (n=18) and MDS (n=4)**

Ongoing Case-Control Studies

Including:

- **IARC**
- **Consortium**

Other Avenues of Research

◆ Other cancers:

- e.g. breast

◆ Non-cancer endpoints:

- e.g., benign thyroid conditions